Congenital central hypothyroidism due to a homozygous mutation in the TSHB gene—just think about it!

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Background
Congenital primary hypothyroidism occurs in about 1 of 3600 life births and is usually detected with newborn screening. Early levothyroxine treatment is the prerequisite for normal psychomotor development of affected children. However, patients suffering from congenital central hypothyroidism are missed by the screening procedure, which may lead to delayed diagnosis and therapy. In very rare cases central hypothyroidism is caused by isolated TSH deficiency due to mutations in the TSHB gene.

Case presentation
Anamnesis
• Poor condition, severe RSV infection at the age of 5 months
• Feeding problems and weight loss, exclusively breastfeeding
• Clinical features: floppy infant, umbilical hernia, meteorism, constipation, icterus prolongatus, short stature
• Developmental delay: Bayley scales of infant development at age 14 months:
  - developmental age of 9-10 months
  - absent speech
  - normal hearing
• Pregnancy and birth: fourth child of healthy, non-consanguineous parents, 40 weeks of gestation, birth weight 3145g, length 50 cm, head circumference 38 cm, pH 7.26
• Social aspects: a 4 months stay in a rehabilitation centre with his mother, physiotherapy is ongoing

Results Therapy
Diagnostics
• Newborn screening: TSH < 0.1 mU/l (NR: <15.0 mU/l)
• Analyses: TSH 0.17 mU/l, fT4 and T3 immeasurable
• Sequencing: TSHB gene: homozygous mutation c.373delT; p.Cys125Valfs*10 (formerly named C105V or 313∆T)

Conclusion
Central hypothyroidism is still a clinical challenge, as it is not detected in newborn screening in Europe while only measuring TSH. Paediatric endocrinologists should therefore advice their paediatric colleagues about this syndrome and its clinical picture. TSHB gene mutations (OMIM 188540) should be considered in cases with very low TSH with preservation of other pituitary axes and normal pituitary MRI.